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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/818,534	03/14/97	NELSON	W 3922

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/818,534	Applicant(s) Nelson et al.
	Examiner Ja-Na Hines	Group Art Unit 1641

☒ Responsive to communication(s) filed on *Jan 19, 1999* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *2 and 9-12* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *2 and 9-12* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Continued Prosecution Application

1. The request filed on December 8, 1998 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/818,534 is acceptable and a CPA has been established. An action on the CPA follows.

2. The amendment filed on January 13, 1999 under 37 CFR 1.312 has been entered. Claims 2 and 9-12 are pending in this office action.

Oath/Declaration

3. This application presents claims for subject matter not originally claimed or embraced in the statement of the invention. A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

New Matter Rejection

4. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 11 recites the characteristic spectrum at 1498 cm^{-1}, however no where in the specification are there any references to 1498 cm^{-1} as the characteristic spectrum. The specification does not clearly teach one skilled in the art to use the method of detecting the presence of a microorganism in a sample using the characteristic spectrum at 1498 cm^{-1}.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2, 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nelson et al. (US 4,487,198) in view of Herron et al. Nelson et al. (US 4,487,198), teaches an apparatus and a method of detection and identification of bacteria by means of ultra-violet excited resonance Raman spectra. The method uses the emitted light energy, which is resonance enhanced Raman scattering and is measured as backscattered energy where the energy processed produces spectra which are characteristic of the bacteria (abstract). The method comprises exciting taxonomic markers in a bacterium with ultra violet light as a lower resonance enhanced Raman back scattered energy; converting the energy to correspond to the taxonomic markers; and displaying the spectra such that the bacterium may be detected and identified (col. 6 lines 43-56).

Nelson et al., teaches an effective range of use being 190-260nm (col. 5 lines 10-15), and further showed five different types of bacteria being excited at 242 nm (col. 5 lines 21-22). The resonance Raman spectra exhibits differences in the composition in the organism, nucleic acids, proteins and other markers are major contributors to the spectra reported (col. 5 lines 22-27). Also rapid analysis is possible, Nelson et al., anticipates a library of spectra will be obtained and can then be rapidly scanned by a computer on the basis of resonance Raman spectra (col 5-6 lines 64-2). The test samples were suspensions of bacterial cultures and other microorganisms can be embodied in any biologically acceptable carrier or medium (col. 6 lines 35-40). However, Nelson et al., does not teach the immobilization of antibodies to a solid phase.

Herron et al., teaches methods for light fluoroimmunoassays where the method specifically teaches capture molecules immobilized to the surface by site specific coupling. Herron et al., teaches the reduction of non specific binding by including a wash step after the sample is incubated with the substrate to remove any unbound tracer molecules (col. 2 lines 54-57). Herron et al., also teaches "..Capture molecules may be whole antibodies, antibody fragments such as Fab' fragments, whole antigenic molecules or antigenic fragments and oligopeptides which are antigenic and/or similar in 3- dimensional conformation to an antibody-binding epitope" (col. 6 lines 39-44). "..The capture molecules may be immobilized on the surface by any method known in the art.." (col. 6 lines 50-51). The method teaches the immobilization of capture molecules on the surface and capture molecules are chosen because of their binding moiety, then the sample solution which contains the analyte molecule binds and a

measurable amount of analyte can then be detected (col. 6 lines 15-26). Finally, Herron et al., provides several tables summarizing the use of solid phase immunoassays using whole antibodies and antibody fragments (col. 13-15, tables I-III).

Therefore, it would have been have been obvious at the time of applicants' invention to have used capture molecules like antibodies immobilized to a solid phase which specifically bind in antibody-antigen complex where the antigen or analyte is a microorganism as taught by Herron et al., in conjunction with a method for detecting the presence of a specific microorganism in a sample as taught by Nelson et al. One would expect reasonable success by employing the effective range of use between 190-260nm which encompasses the range of the instant application and evidenced by the narrowing of the range to 242 since five different types of bacteria are excited at 242 nm as taught by Nelson et al. Further, Nelson et al., teaches that rapid analysis is possible using resonance Raman spectra because it exhibits differences in the composition in the nucleic acids which are major contributors to the spectra reported.

6. Claims 2, 9-10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chadha et al., in view of Herron et al. Chadha et al., teaches the use of ultraviolet micro-Raman spectrograph for the detection of small numbers of bacterial cells. The application of UV resonance Raman spectroscopy is used to selectively excite taxonomic markers to probe and identify bacteria. (page 3088 para.3). Chadha et al., teaches resonance enhancement of the vibrational modes of the bacteria cell components by UV excitation should allow for highly

selective ans sensitive analysis of individual components (page 3088 para. 2). Chadha et al., states that "..Over the past few years resonance Raman spectra of a number of bacteria and bacterial spores, excited at 200-257nm have been reported.."(page 3089 para. 2). "With 242, 252, 257nm excitation, vibrational modes of various nucleosides, nucleic acids, quinones, and calcium dipicolinate are selectively excited.."(page 3089 para. 2). "Nucleic acids have a prominent absorption band around 260 nm, consequently it is not surprising Raman spectra with 257 nm excitation would contain several strong resonance enhanced vibrational modes due to nucleic acids." (page 3092 para. 3). "While resonance Raman cross sections may be large at 257nm, the presence of background fluorescence severely limits the quality of resonance Raman spectra of bacteria,... the absence of overlapping fluorescence in bacterial spectra excited near 242 nm promises better signal to noise even if Raman cross sections are lower." (Page 3092 para. 8). Chadha et al., teaches vibrational modes appearing at 1483 cm^{-1} in different bacterial species (*flavobacterium* and *bacillus*) and these spectra show selectively enhanced modes due to the nucleic acids adenine and guanine (page 3092 para. 3 and 5). Chadha et al., also describes the UV micro-Raman spectrograph (page 3090 para. 2). The experimental conditions Chadha et al., teaches washes the immobilized cells to ensure complete removal of culture medium, and then resuspended the cells in a fluid medium, like phosphate buffer to lower their metabolic activity (page 3091 para. 6).

Herron et al., has been previously discussed. Accordingly, it would have been obvious to one skilled in the art to modify the method and system of Chadha et al., by substituting the

immobilization of antibody to a solid phase because the specificity of antibodies are conventionally used to bind and immobilize bacterial antigens for an assay as taught by Herron et al. Further Chadha et al., teaches the benefits of washing cells and for using nucleic acids as markers because they show strong resonance enhanced vibrational modes and provided better signals over the interference in Raman spectroscopy. The instant application states a wavelength range between 242-257nm, however Chadha et al., teaches the use the exact same wavelengths separately, and benefits for using 242nm (because it promises better signal to noise even if Raman cross sections are lower) and 257nm (because it would contain several strong resonance enhanced vibrational modes due to nucleic acids) and that the wavelengths of 242, 252, 257nm are selectively excited for the vibrational modes of various nucleosides and nucleic acids.

Prior Art

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Howard et al., teaches a resonance Raman method for the rapid detection and identification of Bacteria in water. Raman spectroscopy allows detection of very small quantities of active material in the presence of large amounts of other wise interfering substances (page 73 para. 2). Szoka et al., teaches the use of labels reporter compositions and bound antibodies to comprise a new class of immunoreagents useful in immunoassays (abstract). Szoka et al., teaches immunoassays for virus, bacteria or molecules having more then one epitopic site (col. 10 lines 47-50). The antibody Szoka et al., teaches is immobilized by attachment to a solid

(insoluble) support and at the end of the binding period, the bound analyte is separated and washed (col. 10 lines 54-64). Malmqvist et al., teaches surface plasmon resonance unit and its uses in biosensor systems.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm . The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

James C. Housel 4/26/99

JAMES C. HOUSEL
SUPERVISORY PATENT EXAMINER